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CLINICAL PRACTICE

The Magpie study — clinical implications for poor countries

South African Magpie Trial Collaborators Group

The results of the Magpie Trial, a double-blind randomised controlled trial to assess the role of magnesium sulphate ($MgSO_4$) in preventing eclampsia in women with pre-eclampsia, were published recently.[1] Several South African units were among the 175 hospitals from 33 participating countries. In total, 2 678 of the 10 123 women recruited came from this country. The incidence of eclampsia in the study was 1.9% in the placebo group, compared with 0.8% among women randomised to receive $MgSO_4$. Risk reduction represents a risk reduction of 59%. Put differently, it means that 1 case of eclampsia will be prevented for every 91 women with pre-eclampsia given $MgSO_4$. Risk reduction was influenced by the severity of pre-eclampsia at presentation. The number of patients needed to treat to prevent 1 case of eclampsia was 63 and 109 in those women with severe and non-severe pre-eclampsia respectively. Of the more than 10 000 women, 26% had severe pre-eclampsia and 16% had imminent eclampsia. Only 41% of women in the $MgSO_4$ group who convulsed had their seizure while receiving trial medication. The comparable figure for the placebo group was 56%.

The maternal mortality rate was 316 / 100 000. Of the 31 maternal deaths, 11 occurred in women randomised to receive $MgSO_4$. Although this reduction of 48% was not statistically significant, it may represent a true difference. It is of interest that of the mothers who died, only 1 (2.6%) in the $MgSO_4$ group and 3 (3.2%) in the placebo group had eclampsia. Clearly, the reduction in maternal deaths is not a direct result of the prevention of eclampsia. It may be that $MgSO_4$ has some protective effect on endothelial cell function, which extends beyond its ability to decrease convulsions. In the Collaborative Eclampsia Trial,[2] there were also trends towards fewer deaths among mothers who received $MgSO_4$ rather than either diazepam or phenytoin.[2]

There were some other interesting findings in the Magpie study. There were significantly fewer side-effects in the placebo group (23% v. 4%), while significantly more mothers in the $MgSO_4$ group requested that treatment be stopped early (5% v. 2%). Furthermore, side-effects were significantly fewer in women who received their $MgSO_4$ by the intravenous instead of the intramuscular route (20.3% v. 26.7%).

There was a significant reduction in abruptio placentae in the $MgSO_4$ group (1.4% v. 2.6%). However, there were no other benefits for the baby in terms of Apgar scores, perinatal mortality or admission to neonatal intensive care unit (ICU). It is difficult to explain this in terms of the improved maternal outcome. Clearly the follow-up study of babies born in this trial is of utmost importance.

What are the clinical implications of these results? The African co-workers met during the collaborators meeting in Oxford and prepared a consensus statement. It is agreed that $MgSO_4$ for women with pre-eclampsia reduces the risk of eclampsia, which is small. The use of $MgSO_4$ in specific settings will depend on the capacity to administer it safely, taking into account the site-specific costs and benefits. $MgSO_4$ should be available at all facilities providing services for pregnant women, and health workers should be trained and permitted to administer it. Strategies to identify women with pre-eclampsia and facilities to transfer women to the appropriate level of care must be improved.

The indications for the use of $MgSO_4$ are not so obvious. It was previously clearly shown that eclampsia is an absolute indication for $MgSO_4$.[2] One would probably now add moderate to severe pre-eclampsia as relative indications at the time of delivery and during transport of the patient to a more appropriate level of care. At tertiary level, its administration should also be considered during assessment of women with pre-eclampsia for possible expectant management. The initial dose of $MgSO_4$ is safe, but maintenance doses should only be given when facilities for adequate monitoring of the mother are available. The Magpie study only provides safety data for treatment duration of 24 hours and longer treatment should be undertaken with caution. A loading dose of 4 g should be given by intravenous infusion over 20 minutes. The maintenance doses are 1 g per hour if given by intravenous

The South African Magpie Trial Collaborators Group is made up of South African specialists interested in women's health. All are well known in the field of hypertension in pregnancy and perinatal problems in resource-constrained settings. They are D W Steyn (Tygerberg Hospital); G J Hofmeyr (Cecilia Makiwane and Frere Hospitals); K C Jackson, AKambaran (Mankweng Hospital); P MacDonald (Pretoria Academic Hospital); L Matsela (Medunsa); J Moodley (King Edward VIII Hospital); R C Pattinson (Kalafong Hospital); N E Pirani (Chris Hani Baragwanath Hospital); M G Schoon (Pelonomi Hospital).

infusion or 5 g every 4 hours by intramuscular injection. Maintenance doses should only be given provided that urine output, reflexes and respiration rate are all satisfactory. The preferred way of administration is by intravenous infusion if monitoring of the drip can be done adequately, otherwise by intramuscular injection.

The definitions used in the study for moderate and severe pre-eclampsia are very cumbersome for the clinician. At the collaborators meeting it was suggested that a reasonable working definition of moderate to severe pre-eclampsia be defined as a diastolic blood pressure ≥ 110 mmHg once, or ≥ 100 mmHg persisting after rest, plus proteinuria ≥ 2+ *or* pre-eclampsia with evidence of organ damage (low platelets, rising liver enzymes, deteriorating renal function) or symptoms of severe pre-eclampsia.

Eclampsia is a rare and not entirely preventable condition. The appropriate use of $MgSO_4$ may contribute to improved maternal outcome in women with moderate to severe pre-eclampsia, but the long-term effects on babies need to be investigated further.

1. The Magpie Trial Collaborative Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate?The Magpie Trial: a randomised placebo-controlled trial. *Lancet* 2002; **359:** 1877-1890.
2. The Eclampsia Trial Collaborative Group. Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. *Lancet* 1995; **345:** 1455-1463.

ISSUES IN MEDICINE

The pitfalls of translation — a case study based on the translation of the EQ-5D into Xhosa

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There is an evident need for standardised, internationally recognised instruments to measure health-related outcomes that are also locally applicable. The European Quality of Life 5-Dimensions (EQ-5D) is a widely used measure of health-related quality of life (HRQoL) that was translated into Xhosa. This communication outlines some of the different cultural and linguistic issues that had to be addressed during the translation process.

The translation guidelines provided by the EuroQol group were followed. This involved both forward and backward translations by Xhosa speakers, with consensus meetings after each. Thereafter, lay panel respondent testing of the consensus version was performed.

Eventually a credible Xhosa version of the EQ-5D was produced. Concepts which proved surprisingly difficult to transfer across the languages and cultures included 'mobility', 'confined to bed' and the choice of word to denote 'male'.

The translation process prompted lengthy discussion and proved more challenging than initially anticipated. Despite the rigorous process followed, later additions had to be made to the questionnaire after field testing. It would appear that extreme caution should be exercised when using a questionnaire in a culture and language different from the one in which it was originally developed and validated. If this is not done, the validity of cross-cultural research projects may be open to question.

There is an increasing amount of collaborative and contract research taking place, with the South African arm constituting one of several international country sites. Of necessity the outcome measures are standardised, and the majority of these outcome measures are developed in Europe or North America and then translated for use in other language and cultural groups.

An outcome measure of importance that is often incorporated into research is HRQoL, which can encompass physical and emotional health, functional ability and life satisfaction. The EQ-5D is a generic single index measure that is widely used to measure HRQoL.[1,2] It is a short questionnaire,

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